

AMENDMENTS TO THE CLAIMS

A detailed listing of all claims that are, or were, in the present application, irrespective of whether the claim(s) remains under examination in the application are presented below. The claims are presented in ascending order and each includes one status identifier. Those claims not cancelled or withdrawn but amended by the current amendment utilize the following notations for amendment: 1. deleted matter is shown by strikethrough; and 2. added matter is shown by underlining.

1. (Currently Amended) A synthetic, soluble, endogenous complex comprising ~~formed from~~ at least one component A and at least one component B, whereby component A comprises a binding domain for extra-cellular surface structures that internalize upon binding of component A of said complex, and component B has a constitutive catalytic kinase activity to affect and effects cell biosynthesis and/or signaling ~~including cell death after internalization, wherein the complex is synthetic, soluble, and endogenous.~~

2. (Currently Amended) The complex according to claim 1, whereby the component A is selected from the group of actively binding structures consisting of antibodies, antibody or ~~their derivatives, antibody or~~ fragments thereof, and/or synthetic peptides, ~~such as~~ scFv, mimotopes, ~~and/or chemical molecules such as~~ carbohydrates, lipids, nucleic acids, peptides, vitamins, ~~and/or~~ small molecules with up to 100 atoms with receptor-binding activity ~~such as~~ ligands, ~~in particular single ions, peptidic molecules, non-peptidic molecules, and/or cell surface carbohydrate binding proteins and their ligands such as~~ lectins, ~~in particular~~ calnexins, c-type lectins, l-type lectins, m-type lectins, p-type lectins, r-type lectins, galectins ~~and their derivatives, and/or receptor binding molecules such as~~ natural ligands to the cluster of differentiation (CD) antigens, ~~like~~ CD30, CD40, cytokines, ~~such as~~ chemokines, colony

stimulating factors, type-1 cytokines, type-2 cytokines, interferons, interleukins, lymphokines, monokines, ~~and/or~~ adhesion molecules, including and their derivatives and or mutants, ~~and/or derivatives or combinations of any of the above listed actively binding structures, which bind to CD antigens, cytokine receptors, hormone receptors, growth factor receptors, ion pumps, channel-forming proteins.~~

3. (Currently Amended) The complex according to ~~anyone of~~ claim[[s]] 1 ~~and 2~~, wherein[[by]] component A is selected from the group of passively binding structures consisting of allergens, peptidic allergens, recombinant allergens, allergen-idiotypical antibodies, autoimmune-provoking structures, tissue-rejection-inducing structures, immunoglobulin constant regions and ~~their~~ derivatives, mutants or combinations thereof.

4. (Currently Amended) The complex according to ~~anyone of the~~ claim[[s]] 1 ~~to 3~~, wherein the component A is bound to the extra-cellular surface structure ~~directs the complex to a target cell comprising the binding partner for the binding structures of claims 2 and 3.~~

5. (Currently Amended) The complex according to ~~anyone the of~~ claim[[s]] 1 ~~to 4~~, wherein component A ~~has higher valency by~~ comprises[[ing]] two or more of the binding domains ~~structures selected from anyone of those listed in claims 2 and/or 3.~~

6. (Currently Amended) The complex according to ~~anyone of the~~ claim[[s]] 1 ~~to 5~~, wherein the component B constitutive catalytic kinase activity comprises at least one member of the group consisting of ~~is at least one kinase chosen from the following three classes of kinases: 1. eukaryotic protein kinase (ePK) superfamily,[[2.]]histidine protein kinase (HPK) superfamily and or 3. atypical protein kinase (aPK) superfamily.~~

7. (Currently Amended) The complex according to claim 1 [[6]], wherein the component B constitutive catalytic kinase activity comprises eukaryotic protein kinase comprising the ePK is selected from

(i) a the group of calcium/calmodulin-regulated (CaM) death-promoting kinase[[s,]] that is selected from the group consisting of death-associated protein kinase (DAP-kinase, DAPk), DAP kinase-related protein kinase 1 (DRP-1), also named DAP-kinase 2 (DAPk2), DAP like kinase/Zipper interacting protein kinase (Dlk/ZIP-kinase), ~~also named DAP-kinase 3 (DAPK3)~~ and DAP kinase related apoptosis-inducing kinase (DRAK1 and DRAK2) families,

(ii) a the group of Group of calcium/calmodulin-regulated (CaM) death-promoting kinases-like (CAMKL) family member[[,]] that is selected from the group consisting of ~~at least 49 subfamilies~~, protein kinase AMP-activated alpha 1 catalytic subunit (PRKAA1), protein kinase AMP-activated alpha 2 catalytic subunit (PRKAA2), BRSK1 and BRSK2, CHK1 checkpoint homologue (CHEK1), hormonally upregulated Neu-associated kinase (HUNK), serine/threonine kinase 11 (Peutz-Jeghers syndrome) (STK11), MAP/microtubule affinity-regulating kinase (MARK) 1-4, MARKps 01-30, likely ortholog of maternal embryonic leucine zipper kinase (KIAA0175), PAS domain containing serine/threonine kinase (PASK), NIM1, QIK and SNRK,

(iii) a the group of death-domain receptor interacting protein kinase (RIP-kinase) family[[,]] member that is selected from the group consisting of ~~at least six subfamilies~~, RIP-kinase 1, RIP-kinase 2, RIP-kinase 3 and RIP-kinase 4, ankyrin repeat domain 3 (ANKRD3) and SqK288,

(iv) a the group of multifunctional CaM kinase family, ~~consisting of member that is~~ selected from the group consisting of CaM kinase[[s]] I, CaM kinase II, including the

microtubule affinity-regulating kinases (MARK)₁ and microtubule affinity-regulating kinases-like 1 (MARKL1), CaM kinase IV₁ and CaM kinase kinase subfamilies,

(v) a ~~the group of~~ dedicated CaM kinase[[s,]] selected from the group consisting of Myosin light chain kinase (MLCK), phosphorylase kinase and CaM kinase III,

(vi) a ~~the group of~~ mitogen-activated protein kinase (MAPK) family member selected from the group[[,]] consisting of extracellular signal-regulated kinases (ERK), c-JUN NH2-terminal protein kinases (JNK), nemo-like kinase (NLK) and p38 kinase subfamilies,

(vii) a ~~the group of~~ cyclin-dependent kinase (CDK) family[[,]] member selected from the group consisting of ~~the subfamilies~~, cell cycle related kinase (CCRK), cell division cycle 2 (CDC2), cyclin-dependent kinases (CDK) 1-11, PCTAIRE protein kinase (PCTK) 1-3, PFTAIRE protein kinase (PFTK) 1-2 and cell division cycle 2-like 1 (PITSLRE proteins),

(viii) a ~~the group of~~ eukaryotic translation initiation factor 2-alpha kinase 3 (EIF2AK3) family member, also named (PEK), selected from the group consisting of ~~[[the]]~~ protein kinase interferon-inducible double stranded RNA (dsRNA) dependent (PKR) subfamily, or

(ix) derivatives, mutants or combinations thereof.

8. (Currently Amended) The complex according to claim 1 ~~[[6]]~~, wherein the component B constitutive catalytic kinase activity comprises histidine protein kinase ~~[[is]]~~ selected from ~~a one of the eleven families~~ HPK 1-11 family.

9. (Currently Amended) The complex according to claim 1 ~~[[6]]~~, wherein the atypical protein kinase (aPK) superfamily ~~[[aPK]]~~ comprises

(i) an ~~is selected from the~~ alpha protein kinase family member selected from the group[[,]] consisting of eukaryotic elongation factor-2 kinase (eEF-2k), myosin heavy chain

kinase (MHC-kinase), eukaryotic translation initiation factor 2 alpha kinase 1 (E2K1) and channel kinase (Chak1 and Chak2) subfamilies,

(ii) ~~a the group of~~ Fas-activated s/t kinase (FASTK) family member selected from the group[[,]] consisting of ~~[[the]]~~ FASTK subfamily,

(iii) ~~a the group of~~ protein tyrosine kinase 9 (A6) family member selected from the group[[,]] consisting of A6 and protein tyrosine kinase 9-like (A6r) subfamilies,

(iv) ~~a the group of~~ p21-activated protein kinases (PAK) family member[[,]] consisting of ~~the three highly conserved isoforms:~~ alpha-PAK (PAK1), beta-PAK (PAK3) and gamma-PAK (PAK2, PAKI),

(v) ~~an the group of~~ Interleukin-1 (IL-1)-receptor-associated kinase (IRAK) family member selected from the group[[,]] consisting of IRAK-1, IRAK-2, IRAK-3 and IRAK-4 subfamilies, or

(vi) derivatives, mutants or combinations thereof.

10. (Currently Amended) The complex according to ~~anyone of the claim~~[[s]] 1 ~~[[to 9]]~~, whereby the constitutive kinase activity of component B directly activates or inactivates components of a cell-regulatory pathway[[s]] through ~~[[e.g]]~~. phosphorylation, acetylation, methylation, prenylation, ~~and~~ or sulfation, thereby altering the function, gene expression, or viability of a target cell, ~~whereby the target cell is defined by the binding of that binds~~ component A ~~to it~~.

11. (Currently Amended) The complex according to ~~anyone of the claim~~[[s]] 1 ~~to 10~~, wherein[[by]] component B comprises DAP-kinase 2 (DAPk2) or a derivative thereof.

12. (Currently Amended) The complex according to ~~anyone of the claim~~[[s]] 1 ~~to 10~~, wherein[[by]] component B comprises eukaryotic elongation factor-2 kinase (eEF-2k) or a derivative thereof.

13. (Currently Amended) The complex according to ~~anyone of the claim~~[[s]] 1 ~~to 12~~, comprising

one or more supplementary component S which regulates protein biosynthesis on the transcription and/or translation level, and/or enables purification and/or detection of the complex, and/or facilitates translocation of at least component B into the target cell, and/or intracellular separation and/or activation of component B,

wherein[[by]] the component S is selected from the group of inducible promoters, leader sequences, affinity tags, His tags, translocation domain, amphiphatic sequences and synthetic pro-granzyme B.

14. (Currently Amended) The complex according to ~~anyone of the claim~~[[s]] 1 ~~to 13~~, wherein the components A and B are chemically coupled and/or genetically fused to each other.

15. (Currently Amended) The complex according to ~~anyone of claim~~[[s]] 1 ~~to 14~~, having ~~the~~ comprising amino acid sequence[[s of]] SEQ ID NO: 2, SEQ ID NO: 4 [[and]] or SEQ ID NO: 6.

16. (Currently Amended) A nucleic acid molecule coding for the complex ~~according to anyone of claim[[s 1 to]] 15 or for individual components thereof for the preparation of such complex, and/or a vector comprising said nucleic acid molecule.~~

17. (Currently Amended) A composition comprising a cell or non-human organism after having been transformed or transfected with the nucleic acid molecule or vector according to claim 16, and/or an *in vitro* translation systems synthesizing the complete complex according to anyone of the claims 1 to 15 or individual components thereof.

18. (Currently Amended) The composition of claim 17, wherein the organism or the cell according to claim 17, whereby the organism is either a prokaryote, such as *E. coli*, *B. subtilis*, *S. carnosus*, *S. coelicolor*, and/or *Marinococcus sp.*, or a lower eukaryote, such as *Saccharomyces sp.*, *Aspergillus sp.*, *Spodoptera sp.* and/or *P. pastoris*, a higher non-human eukaryote such as a plant and/or an animal, and the cell is or a primary or cultivated mammalian cell, such as a freshly isolated human cell or a eukaryotic cell line such as CHO, Cos or 293.

19. (Currently Amended) A method for influencing the growth and/or the physiology of [[the]] cells ~~according to anyone of the claims 18 and 19, by~~ comprising culturing the cell[[s]] of claim 17 under conditions supporting the activity of the complex.

20. (Cancelled).

21. (Currently Amended) A medicament comprising Use of the complex of claim[[s]] 1 disposed in a physiologically acceptable dosage form. to 15 and/or the nucleic acid molecule

~~and/or vector of claim 16, and/or the cells and/or non-human organisms of claims 17 or 18, and/or the kit of claim 20 for the preparation of a medicament for the treatment of proliferative diseases, such as cancerous or non-cancerous proliferative diseases, allergies, autoimmune diseases, and/or chronic inflammation.~~

22. (Currently Amended) A medicament comprising the ~~complex according to anyone of the claims 1 to 15, the nucleic acid molecule and/or vector according to claim 16~~ disposed in a physiologically acceptable dosage form, ~~or the cells or non-human organisms according to either one of claims 18 or 19.~~

23. (Currently Amended) A method of altering cell signaling pathways of a targeted cell comprising exposing the cell to ~~Use of the complex according to anyone of the claim[[s]] 1 to 15, and/or of the nucleic acid molecules and/or vectors of claim 16, and/or of the cells and/or non-human organisms of claims 17 or 18, and/or the the kit according to claim 20 for targeted modulation of cellular signaling pathways.~~

24. (Currently Amended) A kinase assay comprising ~~Use of the complex according to any of [[the]] claim[[s]] 1 to 15, of the nucleic acid molecules and/or vectors of 16, and/or of the cells and/or the non-human organisms of claims 17 or 18, for the development of~~ wherein the assay is a prognostic, diagnostic, or [[and]] analytic kinase assay[[s]].

Please add new claims 25 – 30.

25. (New) The complex of claim 1 wherein the constitutive catalytic kinase causes cell death after internalization of the complex into the cell.

26. (New) The complex of claim 2 wherein the component A binds to a cluster of differentiation (CD) antigen, cytokine receptor, hormone receptor, growth factor receptor, ion pump, or channel-forming protein.
27. (New) A vector comprising the nucleic acid molecule of claim 16.
28. (New) A method of treating a cell comprising exposing the cell to the complex of claim 1.
29. (New) The complex of claim 1 wherein components A and B are peptides.
30. (New) A nucleic acid encoding the complex of claim 29.